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10/789,480	02/26/2004	Daniel P. Silver	20363-011 CON	8561

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7590 02/05/2008

EXAMINER

SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
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1636

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02/05/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,480	Applicant(s) SILVER ET AL.	
	Examiner Daniel M. Sullivan	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6, 13-17 and 19-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6, 13-17 and 19-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This Office Action is a reply to the Paper filed 13 November 2007 in response to the Non-Final Office Action mailed 12 September 2007. Claims 1-5, 7-11 and 26-34 were withdrawn from consideration and claims 6 and 12-25 were considered in the 12 September Office Action. Claims 1-5, 7-12, 18 and 26-34 were cancelled and claims 6 and 13-15 were amended in the 13 November Paper. Claims 6, 13-17 and 19-25 are pending and under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 13, 14, 17, 21, 24 and 25 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al. US Patent No. 6,187,994 in view of Qin et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:1706-1710. This rejection is maintained for the reasons set forth in the in the 12 September Office Action (beginning at page 4) and herein below in the response to Applicant's arguments.

Claims 15 and 16 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al. (*supra*) in view of Qin et al. (*supra*) and further in view of Fitzmaurice et al. WO 93/07257. This rejection is maintained for the reasons set forth in the in the 12 September Office Action (beginning at page 8) and herein below in the response to Applicant's arguments.

Response to Amendment Arguments

In response to the *prima facie* rejection of record, Applicant has amended claim 6 to recite that the method is practiced in a plant cell and to include the proviso, "wherein when the sequence excised in said second nucleic acid molecule is a target gene, the expression of said target gene is inactivated". In the remarks filed with the 13 November Paper, Applicant contends

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that claim 6 has been amended to include the subject matter of claim 18 which is not rejected as obvious over Baszczynski et al. in view of Qin et al. According to Applicant, Baszczynski et al. in view of Qin et al. do not teach or suggest the excision of a target gene such that the expression of said target gene is inactivated as required by claim 6. Applicant further contends that claims 15 and 16 are not obvious over Baszczynski et al. in view of Qin et al. and further in view of Fitzmaurice et al. because the claims depend from claim 6 and, according to Applicant, the teachings of Fitzmaurice et al. do not cure the deficiencies of Baszczynski et al. in view of Qin et al. with respect to claim 6.

This argument has been fully considered but is not deemed persuasive. The limitation that Applicant submits distinguishes the invention from the prior art is set forth in the claim as a proviso specifying, "when the sequence excised in said second nucleic acid molecule is a target gene, the expression of said target gene is inactivated". It is noted the claim does not specify that target gene comprised by the second nucleic acid molecule is the same target gene modulated in the method (i.e., "a target gene" recited in the preamble). Therefore, according to the broadest reasonable interpretation of the claims "said target gene is inactivated" of the proviso might refer solely to the target gene of the preamble and does not necessarily require that the target gene excised from the second nucleic acid molecule be inactivated. This is in contrast to previously examined claim 18, which required that the signal sequences in said second nucleic acid molecule flank said target gene so that expression of said recombinase results in excision of said target gene and inactivation of expression of said target gene. Thus, previous claim 18 required that expression of the target gene excised from the second nucleic acid molecule be inactivated.

Baszczynski et al. contemplates an embodiment of the invention wherein the nucleic acid sequence translocated in the method "encode[s] an 'antisense' sequence to turn off or modify gene expression". (Column 7, lines 28-30.) In that embodiment, the sequence excised in the second nucleic acid molecule comprises the target gene in an antisense orientation. When the antisense is translocated such that it is expressed, expression of the target gene that is modulated by the antisense sequence is inactivated. Therefore, the proviso that expression of the target gene is inactivated when the sequence excised in the second nucleic acid molecule is a target gene is met by excision of an antisense target gene from the second nucleic acid molecule and the resulting inhibition of expression of the sense copy of the target gene by the antisense molecule.

Applicant's arguments have been fully considered but are not persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC § 103(a) as obvious over the art.

Rejection of claims 6, 17-23 and 25 under 35 U.S.C. 103(a) as being unpatentable over Anderson *et al.*, US Patent No. 5,629,159 is **withdrawn**. Anderson et al. does not teach or suggest the method practiced in plants.

Rejection of claims 6, 17-22, 24 and 25 under 35 U.S.C. 103(a) as being unpatentable over Anderson *et al.* (*supra*) in view of von Melchner et al. WO 97/07223 is **withdrawn**. Anderson et al. does not teach or suggest the method practiced in plants.

New Grounds Necessitated by Amendment

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 17, 20, 21, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. US Patent No. 6,723,896 B1.

The claims are directed to a method for modulating a target gene in a cell comprising introducing into the cell a first nucleic acid comprising a recombinase gene operably linked to an expression control sequence and signal sequences recognized by a recombinase encoded by the recombinase gene and a second nucleic acid molecule comprising a target gene and signal sequences recognized by the recombinase encoded by the first nucleic acid molecule. The method further requires that the recombinase encoded by the recombinase gene in the first nucleic acid molecule, when expressed in the cell, excises a sequence in the first nucleic acid molecule located between the signal sequences, which excision results in modulation of expression of the

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recombinase gene. In addition, the method requires that the recombinase encoded by the recombinase gene in the first nucleic acid molecule, when expressed in the cell, excises a sequence in said second nucleic acid molecule that is located between the signal sequences in the second nucleic acid molecule and the excision results in modulation of expression of the target gene. Finally, the claims require that the signal sequences for the first and second nucleic acid are not the same sequences.

Moller et al. teaches a method of modulating expression of a target gene in a plant cell comprising introducing a nucleic acid comprising a first nucleic acid sequence comprising a recombinase gene operably linked to an expression control sequence and a second nucleic acid sequence comprising a target gene and signal sequences recognized by the recombinase of the first nucleic acid sequence. The nucleic acid of Moller et al. is configured such that expression of the recombinase in the cell excises a terminator sequence in the second nucleic acid molecule resulting in modulation in expression of the target gene. See especially Figure 1 (reproduced herein below) and the paragraph bridging columns 3-4.

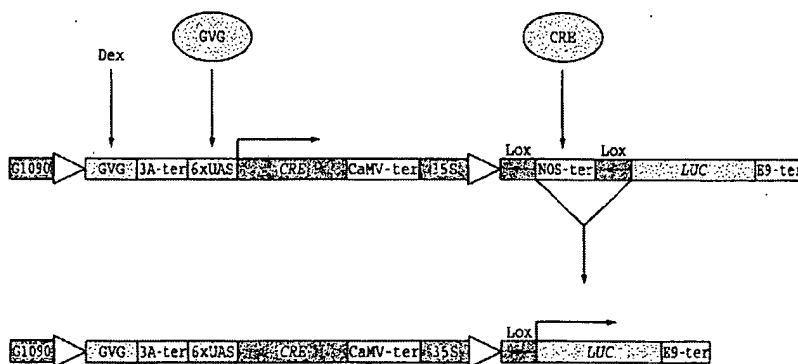


FIG. 1

The method of Moller et al. comprises all of the elements of the method presently claimed except that Moller et al. does not explicitly teach the inclusion of signal sequences recognized by the recombinase in the first nucleic acid molecule such that the expression of the recombinase excises a sequence from the first nucleic acid molecule resulting in modulation of expression of the recombinase gene.

However, Moller et al. further teaches a method "to excise and remove transgenes (e.g., antibiotic resistance markers) from transgenic plants once used and no longer needed. These "suicide" gene cassettes, including the recombination system itself, can therefore be evicted from the plant genome once their function has been exerted." (Column 2, lines 54-59.) This system is illustrated in Figures 4-5, which are reproduced herein below.

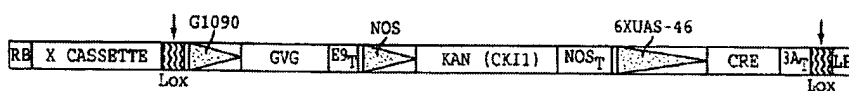


FIG. 4

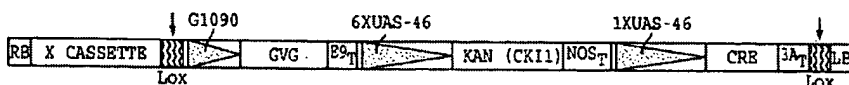


FIG. 5

Note that Moller et al. teaches that the suicide gene cassette comprising the recombinase is included with an "X CASSETTE", which is identified in the caption as a transgene encoding a genetic trait of interest.

It would have been obvious to one of ordinary skill in the art to modify the nucleic acid illustrated in Figure 1 of Moller et al. by the substitution of a suicide cassette comprising a recombinase gene flanked by lox sites such that expression of the recombinase results in excision

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and inactivation of the recombination system as taught in Figures 4-5 and column 2 of Moller et al. One would be motivated to do so in order to obtain the expected benefit of marker gene expression and recombinase activity provided by the suicide cassette and because Moller et al. teaches "The ability to specifically remove transgenes from transgenic plants offers a way of engineering desired genetic traits into crop species without the presence of potentially environmentally unfriendly transgenes such as antibiotic resistance markers." (First paragraph in column 5.) Absent evidence to the contrary, one would have a reasonable expectation of success in combining the elements of the prior art because Moller et al. demonstrates the operability of each system and there is no reason to expect that the elements would not operate together.

In view of the foregoing, the invention of independent claim 6, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Furthermore, the elements of the dependent claims are also found in the teachings of Moller et al. Specifically, the signal sequences in the second nucleic acid molecule are in direct orientation with one another according to the instant claim 17 (see especially Figure 1); the signal sequences in the second nucleic acid molecule flank a negative regulatory element such that expression of the recombinase results in excision of the negative regulatory element and activation of the target gene according to the instant claim 20; the signal sequences in the first nucleic acid flank both the recombinase gene and positive regulatory elements in the recombinase gene according to the instant claims 21 and 22; and the first and second nucleic acid molecules are present in the same vector according to the instant claim 23.

Claims 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. (*supra*).

Claim 19 is directed to the method of claim 6, wherein the signal sequences in the second nucleic acid molecule flank a positive regulatory element of the target gene so that expression of the recombinase results in excision of the positive regulatory element and inactivation of the target gene. As described above, Moller et al. teaches a method wherein a vector having the structure set forth in Figures 4 and 5 is used to regulate the expression of a marker gene comprised within the vector. According to the method, if one construes the marker gene in the vector as the target gene, the signal sequences flank a positive regulatory element and excision of the positive regulatory element (along with the rest of the suicide cassette) results in inactivation of the target gene.

The vector of Moller et al. comprises all of the elements of the first and second nucleic acid molecule of claim 6 except that the same signal sequences are used to excise both the first and second nucleic acid molecule. That is, Moller et al. does not teach that the signal sequences for the first nucleic acid and the second nucleic acid are not the same sequences. However, the difference between the construct used in the claims of the instant application and the construct used in the method of Moller et al. amount to no more than a duplication of parts which would have no effect on the actual functioning of the method as described by Moller et al. Specifically, if one were to include additional lox sites flanking the recombinase gene in the Figure 4 or 5 construct shown above, expression of the recombinase gene would result in excision of the same elements from the genome and would have exactly the same functional effects as in the method practiced without additional lox sites flanking the recombinase gene. In *In re Harza*, 274 F.2d

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669, 124 USPQ 378 (CCPA 1960) the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. (Claims at issue were directed to a water-tight masonry structure wherein a water seal of flexible material fills the joints which form between adjacent pours of concrete. The claimed water seal has a "web" which lies in the joint, and a plurality of "ribs" projecting outwardly from each side of the web into one of the adjacent concrete slabs. The prior art disclosed a flexible water stop for preventing passage of water between masses of concrete in the shape of a plus sign (+). Although the reference did not disclose a plurality of ribs, the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced.). As in *Harza* the claims of the instant application differ from the prior art only by virtue of a duplication of an element (i.e., the lox sites). As the duplication of parts does not produce a new and unexpected result, the instant claims are not patentable over the teachings of the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel M Sullivan/
Primary Examiner
Art Unit 1636